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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,412	07/11/2001	Shohei Koide	109.050US1	8219

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EXAMINER

WESSENDORF, TERESA D

ART UNIT PAPER NUMBER

1639

DATE MAILED: 11/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/903,412

**Applicant(s)**

KOIDE, SHOHEI

**Examiner**

T. D. Wessendorf

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 August 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,4 and 7-50 is/are pending in the application.
- 4a) Of the above claim(s) 9-50 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 8 is/are rejected.
- 7) ☒ Claim(s) 4 and 7 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |  |
|---|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)                        |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____   |

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**DETAILED ACTION**

***Status of Claims***

Claims 1, 4 and 7-50 are pending in the application

Claims 1, 4 and 7-8 are under examination.

Claims 9-50 are withdrawn from consideration as being drawn to non-elected invention.

***Specification***

The objection to the disclosure has been obviated with the amendment to the specification removing the hyperlink.

***Oath/Declaration***

In view of the declaration on the record, the objection is withdrawn.

***Claim Rejections - 35 USC § 112, first paragraph***

The following is a quotation of the first paragraph of 35

U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 8, as amended, are rejected under 35

U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject

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matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide an adequate written description as to the numerous amino acid residues that can be substituted in at least one position of the residues 7, 23 and 9 of the Fn3 molecule. The claimed "another amino acid residue" can read on any kind of natural and/or synthetic amino acids, singly or in combinations, for the different recited positions of the fibronectin type III. There is no defined structure for the type of Fn3 structure in its native or modified state. As evident from the written description in the specification the electrostatic interaction can present an unpredictable effect. For example, the presence of two Cys residues replacing two of the claimed positions 7, 9 and 23 can result in an improper folding consequently, instability of the protein. The specification at e.g., at page 76 provides a description for the specific triads that cause destabilization in the 10<sup>th</sup> region of the Fn module. It also discloses ".....it is not clear why the destabilizing residues are almost completely conserved in Fnfn10. In contrast no other FN3 domains in human fibronectin contain this carboxyl triad. The carboxyl triad of FNfn10 may be

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involved in important interactions that have not been identified to date.....[they] could not perform stability measurements below pH 5 due to protein aggregation, the pH dependence of TnFn3 resembles that of FNfn10....FNfn3 does not contain the carboxylate triad at positions 7, 9 and 23 indicating that the destabilization of TNfn3 at neutral pH is caused by a different mechanism than that for FNfn10...." As factually observed by applicant, there are just too numerous factors, variables and/or mechanisms necessary to identify the destabilizing regions for each kind of Fn in each species. In some species this may not even be present and therefore need not be modified, except for the pH being made acidic, in order to achieve a stabilizing effect. This would appear more complex in an Fn molecule that contains a plurality (e.g., a library of the different beta strands and loops linked by an infinite or unspecified amount of linkers, as claimed). As applicant asserts in the REMARKS (page 16, paragraph one), the substitution of positively charged residues for other residues would not necessarily have a stabilizing effect on a protein. A change in charge of individual amino acid residues would have differing effects on proteins, all of which have unique conformational environments. For example, the newly cited Dao-pin is stated to teach that the introduction of an attractive electrostatic interaction has

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small effects on protein stability. The specification specifically defines the residues that can replace the amino acids in the recited positions that retain a favorable electrostatic interaction. There is not enough guidance or direction provided to a skilled in the art as to the other amino acid residues that can replace the triad residues. It does not describe how one can chose or pick from the numerous existing natural or synthetic residues the triad residues. This is made more complex as the Fn structure is not clearly set forth. A "written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials". University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405( 1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993)[The claims at issued in University of California v. Eli Lilly defined the invention by function of the claimed DNA (encoding insulin)]. Thus, at the time of applicants' invention, applicants appear not to be in possession of the huge scope of any amino acid residue replacing any of the three recited positions in any type of Fn structure. [This rejection may be overcome by incorporating the limitation of claims 4 and 7 to claim 1.]

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In view of the cancellation of claims 51-53, the rejection under this statute no longer applies.

***Claim Rejections - 35 USC § 112, second paragraph***

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation that Asp 7, 23 and Glu9 have been deleted appears at odd with the base claim 1. The base claim recites substitution, not deletion. If these residues are deleted then, it is unclear as to the need for substitution.

In view of the cancellation of claims 51-52, the double patenting rejection no longer applies. Also, with the amendments to claim 1, the rejection under 102 and 103 has been obviated.

***Allowable Subject Matter***

Claims 4 and 7 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form i.e., included in claim 1.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is

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reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

This application contains claims 9-50 drawn to a nonelected invention. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

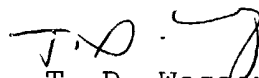
Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571)272-0812. The examiner can normally be reached on Flexitime.



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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
T. D. Wessendorf  
Primary Examiner  
Art Unit 1639

tdw  
November 12, 2004